trimETHOPRIM WITH SULFAMETHOXAZOLE

Indication

- Treatment of infections due to susceptible gram-positive and gram-negative organisms (particularly those of urinary, respiratory and gastrointestinal tract[1])
  - Not recommended for infants less than 4 weeks of age as theoretical risk of kernicterus due to bilirubin displacement from plasma albumin
- Treatment or prophylaxis of *Pneumocystis jirovecii* pneumonia (PJP)
- HIV exposed infants (from 4–6 weeks of age) born to mothers living with HIV, until HIV excluded[2] (in consultation with infectious disease specialist)

ORAL

Presentation

- Oral solution: 40 mg trimethoprim and 200 mg sulfamethoxazole in 5 mL
  - Use trimethoprim component (mg) for prescribing

Dosage

Indication	Dose	Frequency
UTI prophylaxis[3,4]	2 mg/kg	once daily
HIV exposed[2] (PJP prophylaxis)	20 mg (NOT per kg)	once daily
Mild-moderate infection[3]	4 mg/kg	every 12 hours

Preparation

- Shake bottle vigorously
- Draw up prescribed dose into oral/enteral syringe

Administration

- Oral/OGT/NGT with feeds (to reduce gastric upset[3])

INTRAVENOUS

Presentation

- Ampoule:80 mg trimethoprim and 400 mg sulfamethoxazole in 5 mL
  - Use trimethoprim component (mg) for prescribing and dilution calculations

Dosage

Indication	Dose	Frequency
Severe infection/immunosuppressed[4]	2–3 mg/kg	every 6 hours
PJP treatment[5,6] *(adapted from 15–20 mg/kg daily)*	3.75–5 mg/kg	every 6 hours

Preparation (if NOT fluid restricted)

- Draw up 32 mg (2 mL) from the 5 mL trimethoprim vial and make up to 50 mL total volume with compatible fluid[7]
  - *Concentration now equal to 0.64 mg/mL*

Preparation (if fluid restricted)

- Draw up 32 mg (2 mL) from the 5 mL trimethoprim vial and make up to 30 mL total volume with 5% glucose[7] (only 5% glucose[8])
  - *Concentration now equal to 1 mg/mL*
- Maximum solution concentration[7] is 1 mg/mL
- Use within 30 minutes of preparation as precipitation can occur within 2 hours[8]

Administration

- Draw up prescribed dose plus sufficient to prime the infusion line
- Prime the infusion line and reduce syringe to prescribed volume
- IV infusion via syringe driver pump
  - For 0.64 mg/mL solution infuse over 1–1.5 hours[8]
  - For 1 mg/mL solution infuse over 1 hour (for stability reasons)[8]
- On completion
  - Disconnect syringe and infusion line
  - Flush access port at same rate as infusion

Special considerations	• Cautions o The long-acting sulphur drug in trimethoprim sulfamethoxazole causes release of bilirubin from protein carrier sites in plasma–evaluate use, particularly if premature, or if ABO or Rh D blood group incompatibility exists[3] o Sulfonamides increase the risk of haemolysis in G6PD deficiency[3] o Renal impairment increases risk of hyperkalaemia–reduce dose to avoid sulfamethoxazole accumulation[3] o Low urine pH increases risk of crystalluria (sulfamethoxazole poorly soluble at low pH)[3] o Hepatic impairment may increase risk of adverse effects[3] o If fluid restricted, may be administered undiluted via CVC[8]
Monitoring	• Signs of jaundice[3] • Serum potassium, FBC, renal function (for IV, high dose, renal impairment)[3] within first week, then at SMO discretion • Extravasation risk (pH 10)[7]
Compatibility	• Fluids o 5% glucose[8], 10% glucose[8], 0.9% sodium chloride[8] • Via Y-site (may be variable compatibility at different drug concentrations) o Aciclovir[8], dexmedetomidine[8], esmolol[8], filgrastim[8], granistron[8], hydromorphine[8] magnesium sulfate[8], morphine sulfate[8], piperacillin-tazobactam[8], vecuronium[8], zidovudine[8]
Incompatibility	• Fluids o No information[8] • Drugs (at dilutions specified above) o Caspofungin[8], midazolam[8] • Do not add to or mix with any other agent[9]
Interactions	• Digoxin: increased risk of digoxin toxicity[1] • Amiodarone, chloral hydrate, clarithromycin, erythromycin, flecainide, fluconazole, octreotide, increased risk of cardiotoxicity (QT prolongation, torsades de pointes, cardiac arrest)[1] • Leucovorin calcium (folinic acid): increased rate of trimethoprim treatment failure[1] • Phenytoin: increased risk of phenytoin toxicity[1] • Spironolactone: increased risk of hyperkalaemia[1] • Zidovudine: increased serum concentration of zidovudine[1]
Stability	• Oral solution o Store below 25 °C[10]. Protect from light[10] o Discard according to expiry date on bottle • Ampoule o Store below 30 °C.[9] Do not refrigerate.[9] Protect from light[9] o Do not use if cloudy or crystallised[9]
Side effects	• Hypersensitivity reactions: fever[3], rash[3], eosinophilia[3], Stevens-Johnson syndrome[3], toxic epidermal necrolysis[3], hepatitis[3], interstitial nephritis[3], systemic vasculitis[3], pancytopaenia[3] • Blood pathology: hyperkalaemia[3], blood dyscrasias[3] (e.g. neutropaenia) thrombocytopaenia[3] (rarely significant); (rarely) hypoglycaemia[3], hyponatraemia hepatitis[3], megaloblastic anaemia[3], methaemoglobinaemia[3], aseptic meningitis • Digestive: (common) vomiting[3], diarrhoea[3]; prolonged use may cause *Clostridioides difficile*-associated disease[3], fungal overgrowth[3] • Integumentary: (rare) erythema[3] • Nervous: (infrequent) drowsiness[3] • Urinary: (rare) crystalluria[3], urinary obstruction with anuria/oliguria[3]
Actions	• Trimethoprim and sulfamethoxazole (co-trimoxazole) competitively inhibit bacterial folate production essential for bacterial growth[3] • Collectively block two consecutive steps in the biosynthesis of nucleic acids and proteins essential to many bacteria[1] • Rapidly and well absorbed from the gastrointestinal tract[1]

Abbreviations	CNS: central nervous system, CVC: central venous catheter, FBC: full blood count, HIV: human immunodeficiency virus, IV: intravenous, OGT: orogastric, NGT: nasogastric, PJP: *Pneumocystis jirovecii* pneumonia, SMO: most senior medical officer, UTI: urinary tract infection
Keywords	Synthetic antibacterial agent, cotrimoxazole, sulfonamide, neonatal sepsis, *Pneumocystis jirovecii* pneumonia, PJP

The Queensland Clinical Guideline *Neonatal Medicines* is integral to and should be read in conjunction with this monograph. Refer to the disclaimer. Destroy all printed copies of this monograph after use.

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